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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,765	10/02/2003	George N, Serbedzija	018852-000511US	1627

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EXAMINER	
BERTOGLIO, VALARIE E	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,765	SERBEDZIJA ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31,33 and 35-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,33 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10/02/2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *02/08/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply dated 02/02/2007 has been entered. Claims 1-30,32 and 34 have been cancelled. Claim 31 has been amended. Claims 31,33 and 35-38 are pending and under consideration in the instant office action.

Specification

The objection to the specification is withdrawn in light of Applicant's amendment updating the status of priority applications.

Drawings

The objection to the drawings is withdrawn in light of Applicant's amendment to the description of Figure 17.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) was denied as set forth at page 4 of the office action dated 08/03/2006. The effective filing date granted for the claims is 02/22/1999 based on support in US Application 09/255,397. Applicant has argued that the '783 application does support screening agents for toxicity by assaying gene expression. However, the support alleged by Applicant is directed to screening for toxicity of a compound by assaying morphological traits such as developmental delay, pericardial edema, and minor axial defects. '783 does not provide support for screening compounds by assaying for gene expression changes.

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

The rejection of claims 31,33 and 35-38 under 35 U.S.C. 112, first paragraph, enablement is withdrawn in light of Applicant's amendments to the claims.

The following new rejection is necessitated by amendment.

Claims 31,33 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening an agent for toxic activity comprising administering an agent to a teleost in vivo, processing in vitro or in situ said embryo in a manner to detect expression of a protein or mRNA in a specific organ or tissue, and quantifying mRNA or protein expression, wherein a change in said mRNA or protein expression in comparison to that of a control teleost embryo not administered the agent is indicative of toxic activity of the agent, does not reasonably provide enablement for screening an agent for a desired activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404).

Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Applicant has amended claim 31 to include, in addition to screening for toxic activity of an agent, screening for desired activity of the same agent in the same fish. The specification does not provide enabling teachings and guidance necessary to know how to carry out screening for a desired activity or what in intended to be desired. It is noted that, because the specification fails to define "desired activity" the breadth of the claims encompass toxic activity as being a desired activity. Applicant points to the specification at page 31, lines 24 and 25 and page 65, lines 7-21 in support of the claim amendment. Page 31 recites that the method is useful in identifying contra indications to therapeutic value of a compound. This indicates that a known therapeutic agent is being screened for toxic effects. It does not support screening an agent for a therapeutic effect (note, this appears to be the subject matter of US 6,656,449). The specification does not support the concomitant screening of an agent for a therapeutic and toxic effect. To screen for a therapeutic activity, a disease state to be remedied or an effect of the agent to be screened must

be known. The specification does not teach what activity is a desired activity or how to screen for such an activity. The claims are drawn to use of a wildtype teleost. It is not known how to screen for a "therapeutic" agent a normal, wild-type teleost. Other embodiments of "desired effect" are not supported by the specification. Page 65 discusses screening for both desired and undesired effects of an agent, however, the focus, again, is on screening for toxicity or undesired effects. Lines 16-21 refer to the toxic effects of drugs. It appears that the support in the specification regarding the combination of desired and toxic effects of an agent are drawn to screening the toxic effects of agents known to have a desired effect and are not drawn to screening for a desired effect. It is noted, that "desired" is not defined by the specification and encompasses any activity, including toxic activity.

It is also noted that the last step of the claimed method of claim 31 is further not enabled in that the step fails to recite what result is indicative of promoting the desired activity and how such an activity is assessed. The claim defines how to assess toxic activity by way of screening for changes in gene expression as a result of the agent. Such a defined methodology is not set forth for assessing the "desired activity". One of skill in the art would not know how to carry out the method step as broadly claimed.

Enablement

The rejection of claims 32 and 34 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is rendered moot by the cancellation of the relevant claims.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of claims 31-38 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicant's amendments to the claims.

The following new rejection is necessitated by amendment.

Claims 31,33,35-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 31, the phrase "detecting a change in vitro or in situ" is unclear because it is not known whether the change in expression occurs in vitro (or in situ) or if the change in expression occurs in vivo and is detected in vitro or in situ. Claims 33 and 35-38 depend from claim 31.

Claim 31 recites the limitation "the teleost" in line 7. There is insufficient antecedent basis for this limitation in the claim. It is not clear to which teleost "the teleost" is referring. Claims 33 and 35-38 depend from claim 31.

Claim 33 recites the limitation "the response" in line 7. There is insufficient antecedent basis for this limitation in the claim. The term "the response" has been deleted from claim 31.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31,33 and 35 remain rejected under 35 U.S.C. 102(b) as being anticipated by Mizell [1997, IDS]. The rejection is maintained for reasons of record set forth at pages 8-9 of the office action dated 08/03/2006.

As set forth above, priority to US provisional applications 60/075,783 and 60/100,950 for the instantly claimed subjected matter has been denied. The effective filing date is 02/22/1999.

Applicant has amended claim 31 to add a step of assessing whether the agent is effective to "promote the desired activity". As set forth above in the rejection under 35 USC 112, 1st paragraph, enablement, what is defined as a "desired activity" is not clearly set forth by the specification. When broadly interpreted, a desired activity can be any activity, and therefore, Mizell continues to anticipate the claimed method.

Mizell taught a method for screening an agent for toxic activity in both zebrafish and medaka, which are teleosts. Mizell taught administering the agent (TCDD, toluene, benzene) to multiple (claim 35) dechorinated zebrafish embryos and detecting toxic effects by monitoring CYP1A activity (see page 416, last paragraph-page 416, paragraph 2, page 419, col. 2, paragraph 2; see Table 5, line 2 at page 96 of the specification). Early activation of CYP1A was shown as an indicator of TCDD toxicity. Multiple embryos were assayed at a time (page 421, col. 2, paragraph 4), meeting the limitations of claim 35. Mizell taught that toxic activity is detected after a 30 minute exposure to TCDD (page 415, col. 2, paragraph 2), which constitutes detecting toxicity over time at a predetermined interval as required by claims 32 and 34. Mizell observed

changes in heart formation as well as Cyp1A activity in both the gut and liver, fulfilling the limitations of claim 33.

Applicant's arguments have been fully considered and are not persuasive.

Applicant argues that Mizell does not suggest screening a desired activity and is concerned with use of a zebrafish as a sentinel for aquatic pollution. While it is agreed that the purpose of the teachings of Mizell appears to be different from that of the instant claims, the claims fail to establish a patentable difference between the method claimed and those of Mizell. Applicant is encouraged to point to support in the specification that differentiates the instant claims from those of Mizell by clearly defining what is intended by a "desired activity" and clearly setting forth each of the necessary method steps. Otherwise, screening for toxic activity can be broadly interpreted as qualifying as screening for a desired activity.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizell (1997) as applied to claims 31-35 above, and further in view of Terse [1993, Toxicon, 31:913-919]. The rejection is maintained for reasons of record set forth at pages 9-10 of the office action dated 08/03/2006 and for reasons of record as explained under the preceding rejection under 35 USC 102(b). Applicant's remarks are addressed above as well.

Conclusion

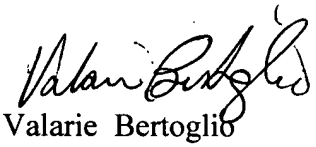
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Valarie Bertoglio
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Art Unit 1632